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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,707	09/30/2003	May Tom-Moy	10031347-1	8124

7590 03/17/2006  
AGILENT TECHNOLOGIES, INC.  
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EXAMINER

LUM, LEON YUN BON

ART UNIT PAPER NUMBER

1641

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/676,707

Applicant(s)

TOM-MOY ET AL.

Examiner

Leon Y. Lum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. The amendment filed December 27, 2005 is acknowledged and has been entered.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 8, 10-11 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Eggers et al (US 5,670,322).

Eggers et al reference teaches an array of test sites 14 (i.e. plurality of features), each test site comprising a well 20 in an insulating layer 22 (i.e. pad of resistive material) with first and second plates 24a-b formed on two sides of the well to serve as a localized electrode pair, a probe 26 attached to the bottom of the well (i.e. probe disposed between first and second electrode), and detection circuitry 16 on-chip that addresses each test site (i.e. integrated addressing circuitry allows interrogation of features). See column 3, line 63 to column 4, line 53; and Figures 1 and 2a-b.

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With regards to claim 10, Eggers et al teach recognition circuitry 18 (i.e. measurement circuitry) connected to the detection circuitry 16. See column 3, lines 63-66 and Figure 1.

With regards to claim 11, Eggers et al teach that other circuitry for processing information may be provided (i.e. circuitry for storage of data). See column 4, lines 31-33.

With regards to claims 13-14, Eggers et al teach that different probes are used in test sites 14 for simultaneous detection of a plurality of different targets (i.e. each of plurality of different features comprises a different probe), wherein the probes are oligonucleotides (i.e. polynucleotides). See column 4, lines 7-11.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) in light of Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000), and in view of Eggers et al (US 5,891,630).

Park et al reference teaches the electrical detection of DNA by detecting binding between a capture oligonucleotide strand located in the gap between two fixed microelectrodes and a longer target oligonucleotide in solution (i.e. contacting feature with sample; probe disposed between first and second electrode; polynucleotide). See page 1503, middle column, 2<sup>nd</sup> paragraph to right column, 1<sup>st</sup> paragraph. Park et al also teach an array of 4 electrode pairs with a different oligonucleotide capture strand in the electrode gap (i.e. microarray with a plurality of features; plurality of targets are detected). See page 1503, right column, 3<sup>rd</sup> paragraph to page 1504, left column, 1<sup>st</sup>

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paragraph. In addition, Park et al teach the step of increasing the sensitivity of the device by exposing the active component of the device to a solution of Ag(I) and hydroquinone (i.e. applying a source of metal ions). See page 1503, right column, 2<sup>nd</sup> paragraph. Park et al further teach capacitance or conductivity measurements to determine the number of target molecules that fill the gap (i.e. analyzing the results to detect the target). See page 1503, right column, 2<sup>nd</sup> paragraph. Furthermore, Park et al teach measuring the resistance value across the gaps with a Fluke 189 multimeter (i.e. select one of the plurality of features to be interrogated; measuring the observable property at the selected feature). See page 1504, left column, 3<sup>rd</sup> paragraph to middle column, 1<sup>st</sup> paragraph. Since the Fluke 189 multimeter can only perform one measurement at a time, the detection of the 4-electrode pair array necessarily requires sequential detection, which indicates that the electrode pairs are selectively interrogated (i.e. repeating steps (c) and (d) to selectively interrogate each of the plurality of features). See Fluke Corporation, pages 2-4, 2-17, 3-6, and 3-7.

However, Park et al fail to teach that the substrate comprises integrated addressing circuitry in operable relation to each of the plurality of features and also fail to teach the step of providing a signal to the addressing circuitry to select one of the plurality of features to be interrogated.

Eggers et al reference teaches detection circuitry 16 on-chip, wherein a varying signal of frequency can be applied to each site, in order to enable fast detection of hybridization for large DNA probe arrays. See column 4, lines 16-18; column 7, lines 30-32 and lines 44-46; and Figure 1.

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It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method and apparatus of Park et al with detection circuitry 16 on-chip, as taught by Eggers et al, in order to enable fast detection of hybridization for large DNA probe arrays. The detection circuitry of Eggers et al therefore provides an advantage over the multimeter of Park et al since the detection circuitry is able to interrogate a large number of electrode pairs in a short amount of time, whereas the handheld multimeter of Park et al would require a large amount of time to test each electrode pair in a large array. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the detection circuitry of Eggers et al, in the apparatus of Park et al, since Park et al teach dual electrodes to detect hybridization in an array, and the detection circuitry of Eggers et al is connected to a plurality of electrode pairs that also detect hybridization. With regards to claims 3-5, Park et al teach that the target oligonucleotide is attached to Au nanoparticles at one end (i.e. gold nanoparticle label) and that Ag(I) and hydroquinone is added after the binding of target and capture oligonucleotides (i.e. attaching a label to target prior to applying the enhancement reaction; deposits metal). See page 1503, right column, 1<sup>st</sup> paragraph; and Figure 1 and caption.

8. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) in light of Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000), and in view of Eggers et al (US 5,891,630) as applied to claims 1 and 3 above, and further in view of Cheung (US 5,132,242).

Park et al and Eggers et al references have been disclosed above, but fail to teach that the label is attached to the target via a biotin-avidin conjugate binding pair.

Cheung reference teaches conjugation of DNA to microspheres using avidin and biotin, in order to take advantage of the strong non-covalent interaction between avidin and biotin. See column 10, lines 46-53.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Park et al and Eggers et al with conjugation of DNA to microspheres using avidin and biotin, as taught by Cheung, in order to take advantage of the strong non-covalent interaction between avidin and biotin. The avidin-biotin conjugation to connect DNA to microspheres, as taught by Cheung, provides an advantage over the oligonucleotide-modified particles of Park et al and Eggers et al, since the avidin-biotin conjugation provides a strong interaction that would not allow dissociation of the microspheres from the bound targets and result in false negatives. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the avidin and biotin binding pairs, as taught by Cheung, in the method of Park et al and Eggers et al, since Park et al and Eggers et al teach particles bound to nucleic acids, and the avidin and biotin binding pairs of Cheung are able to conjugate microspheres, a type of particle, to nucleic acids.

9. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eggers et al (US 5,670,322) in view of Nayak (US 4,789,628).



Eggers et al reference has been disclosed above, but fails to teach that the pad of resistive material comprises a plurality of segments with fissures between the segments.

Nayak reference teaches a plurality of spaced projections within a well with probes immobilized thereon, in order to increase the surface area for specific binding in assays that may have a low concentration of substances. See column 3, line 51 to column 4, line 10; and column 6, line 62 to column 7, line 19.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Eggers et al with a plurality of spaced projections within a well with probes immobilized thereon, as taught by Nayak, in order to increase the surface area for specific binding in assays that may have a low concentration of substances. By replacing the planar surface of Eggers et al with the projections of Nayak, the apparatus of Eggers et al would have the advantage of being able to detect specific binding with a sample solution having a low concentration of target. This advantage therefore provides the motivation to combine the projections of Nayak in the apparatus of Eggers et al. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in including the projections of Nayak in the apparatus of Eggers et al, since Eggers et al teach probes immobilized on a surface for assay purposes, and the projections of Nayak are one example of a surface that can immobilize probes for an assay.

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10. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eggers et al (US 5,891,630) in view of Mallet et al (US 6,660,533 B2).

Eggers et al reference has been disclosed above, but fails to teach that the pad of resistive material is metal oxide.

Mallet et al reference teaches metal oxides surfaces, in order to provide an immobilization that is engenders very good signal to background noise ratios, and stable immobilization. See column 2, lines 45-53.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Eggers et al with metal oxides surfaces, as taught by Mallet et al, in order to provide an immobilization that is engenders very good signal to background noise ratios, and stable immobilization. By providing good signal to background noise ratios, the binding of Eggers et al would be more accurately detected. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the metal oxide surfaces of Mallet et al, in the apparatus of Eggers et al, since Eggers et al teach biomolecule immobilization onto surfaces, and the metal oxide of Mallet et al is one type of surface that can immobilize biomolecules.

11. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eggers et al (US 5,891,630) in view of Sandstrom (US 6,545,758 B1).

Eggers et al reference has been disclosed above, but fails to teach at least one reference feature in operable relation to the addressing circuitry.

Sandstrom reference teaches control sites on a microarray, in order to compare experimental probe sites to a reference or purposefully mismatched site for eliminating signal from background signal and nonspecific hybridization. See column 4, line 61 to column 5, line 17.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Eggers et al with control sites on a microarray, as taught by Sandstrom, in order to compare experimental probe sites to a reference or purposefully mismatched site for eliminating signal from background signal and nonspecific hybridization. The control sites of Sandstrom therefore provide the advantage of determining accurate detection in the binding sites of Eggers et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including control sites, as taught by Sandstrom, in the apparatus of Eggers et al, since Eggers et al teach an array of binding sites, and the control sites of Sandstrom can also be placed in an array of binding sites.

### ***Response to Arguments***

12. Applicants' arguments, see page 5 of the Response, filed December 27, 2005, with respect to claim 7 have been fully considered and are persuasive. The rejection under 35 U.S.C. 112, 2<sup>nd</sup> paragraph of claim 7 has been withdrawn.

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13. On pages 6-7 of the Response, Applicants traverse the rejection of claims 8-11 and 13-14 under 35 U.S.C. 102(b) as being anticipated by Eggers et al, and also traverse the rejection of claims 1-7, 12, and 15 under 35 U.S.C. 103(a) in view of Eggers et al and several secondary references. Applicants present only one reason for the traversals: the references do not teach the limitation "a pad or resistive material disposed between the first electrode and the second electrode". Specifically, Applicants argue that the Examiner's interpretation of element 22 in Eggers et al, as applied in the previous Office action, is incorrect. Applicants submit that element 22 is an "insulating material" and not the claimed resistive material of the instant invention. See page 6, 2<sup>nd</sup> paragraph. Furthermore, Applicants state that the secondary references do not remedy the alleged failings of Eggers et al and therefore, none of the applied references teach the claimed limitation.

Applicants' argument has been fully considered, but is not persuasive. Applicants are correct in stating that element 22, as disclosed by Eggers et al, is an insulating material. Eggers et al teach that a preferred material is silicon dioxide. See column 4, lines 44-45. However, the fact that element 22 is considered to be an insulating layer does not prevent it from being applied against the claimed "resistive pad". Applicants specifically state in the disclosure that ["Resistive", as used herein in referring to a "resistive pad" or a "pad of resistive material", means that the pad resists the flow of electric current through the material]. See page 10, lines 28-29. Since Applicants can be their own lexicographers, any definition of a term in the specification is considered to limit the scope of that term as claimed. Therefore, the "resistive pad" of

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the instant claims is considered to be **any** material that **resists** the flow of electric current, which has a scope broad enough to encompass materials that completely prevent the flow of electric current. A material that completely prevents the flow of an electric current would inherently resist the current. Applicants submit that the silicon dioxide of Eggers et al, while not specifically disclosed as completely blocking the flow of current, is different from the “resistive pad” because silicon dioxide is an insulator and blocks electric current flow, thereby implying that the silicon dioxide completely blocks current flow. However, the definition of “resistive pad” in the specification includes silicon dioxide since an insulator, even assuming that it completely blocks current flow, would by definition perform the effect of resisting electric current by blocking current flow.

Even if the claimed “resistive pad” is required to be a material that provides at least some electric current flow, the silicon dioxide insulator of Eggers et al would still be applicable. In the specification, Applicants disclose that in addition to “resistive material”, the substrate can also be a “non-conductive material”, which allows a less than about 0.5% of electric flow. See page 10, last paragraph, lines 4-7. It is understood that by providing definitions for the terms “resistive” and “non-conductive”, Applicants are making the distinction that the “resistive pad” is a material that is conductive and allows more than about 0.5% of electric flow. Applicants also define “non-conductive” in terms of its resistance, by stating that a material is “defined to be non-conductive when the measured resistance between two electrodes of a test apparatus is greater than about 100 megaohms.” See page 11, 2<sup>nd</sup> paragraph.

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Therefore, any material that is considered to be conducting has a resistance of less than or equal to about 100 megaohms. It is well known in the art that silicon dioxide has a resistivity of  $10^{10}$  ohm-cm. See Kurtz et al (US 3,930,823), column 4, lines 17-18. Since Eggers et al teach that an electrode pair is located on either side of a well, and the wells are 1 mm in diameter (see column 8, line 51), a silicon dioxide with an inherent resistivity of  $10^{10}$  ohm-cm, would provide a resistance of  $10^9$  ohm, or 1 megaohm. One of ordinary skill in the art at the time of the invention would recognize that 1 megaohm is substantially different from the disclosed "about 100 megaohms" in the specification. Therefore, even if the claimed "resistive pad" is required to be a material that provides some amount of electric current flow, since silicon dioxide does not meet the criteria for a non-conducting material as defined by the specification, it is considered to be a resistive material that reads on the "resistive pad".

In light of the arguments above, the rejections made in the previous Office Action with respect to claims 1-8 and 10-15 are maintained. Claim 9 has been amended such that a new grounds of rejection is necessary, as provided supra.

### ***Conclusion***

14. No claims are allowed.

15. Applicant's amendment, specifically to claim 9, necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

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See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

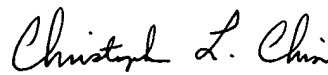
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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum  
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